Human ESC Self-Renewal Promoting miRNAs Induce Epithelial-Mesenchymal Transition in Hepatocytes by Controlling the PTEN and TGFbeta Tumor Suppressor Signaling Pathways.

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Public Summary:
The self-renewal capacity ascribed to embryonic stem cells (ESC) is reminiscent of cancer cell proliferation, raising speculation that a common network of genes may regulate these traits. A search for general regulators of these traits yielded a set of microRNAs for which expression is highly enriched in human ESCs and liver cancer cells (HCC) but attenuated in differentiated quiescent hepatocytes. Here, we show that these microRNAs promote hESC self-renewal, as well as HCC proliferation, and when overexpressed in normally quiescent hepatocytes, induce proliferation and activate cancer signaling pathways. Proliferation in hepatocytes is mediated through translational repression of Pten, Tgfbr2, Klf11, and Cdkn1a, which collectively dysregulates the PI3K/AKT/mTOR and TGFβ tumor suppressor signaling pathways. Furthermore, aberrant expression of these miRNAs is observed in human liver tumor tissues and induces epithelial-mesenchymal transition in hepatocytes. These findings suggest that microRNAs that are essential in normal development as promoters of ESC self-renewal are frequently upregulated in human liver tumors and harbor neoplastic transformation potential when they escape silencing in quiescent human hepatocytes.

Scientific Abstract:
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